THERMOTHERAPY IN DERMATOLOGIC INFECTIONS

Essay
Submitted for partial fulfilment of Master Degree in Dermatology, Venereology, and Andrology

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Introduction

Thermotherapy has long been used as an adjuvant therapy and a healing modality for treatment of several infections that may be resistant to standard antimicrobial therapy, yet its utility in the modern era is under estimated and is worth revisiting ***(Doherty et al.,).*** Although thermotherapy implies the use of heat, it also includes the use of cryotherapy. The rationale for treatment of infections with thermotherapy whether with heating or freezing has been studied by many throughout the last decades, yet the exact mechanism is not entirely clear, although there is evidence that thermotherapy may involve direct toxic effects on microbes and/or up-regulation of immune response to infectious agents ***(Reithinger et al., and Lobo et al.,).***

Several dermatologic infections including chromomycosis, sporotrichosis, cutaneous leishmaniasis, acne, viral and mycobacterial infections have proven sensitive to induced local use of cryotherapy or hyperthermia utilizing hot packs, electctric bed warmers, ultrasound waves, infrared lasers particularly the CO_2 laser and Nd:YAG laser in addition to radiofrequency ***(Doherty et al.,).***

Studies have also proved that cryotherapy is effective as an adjuvant therapy in the treatment of blastomycosis-like pyoderma not responding to treatment with cotrimoxazole alone ***(Castro et al., , Asillian et al., and Su o et al.,).***

Although it is considered as a simple and safe adjuvant treatment that is well tolerated by most patients, its value in the treatment of many dermatologic infections is under estimated ***(Willard et al.,).***

Aim of the Work

The aim of this essay is to review the rationale behind the use of thermotherapy in treatment of dermatologic infections, and to discuss its clinical approach in treatment of infections whether alone or as an adjuvant with other lines of therapy.

Thermotherapy

Thermotherapy is the therapeutic application of heat or cold to treat a disease and relieve its associated symptoms whether alone or as an adjuvant with various established treatment modalities ***(Nadler et al.,*** ***).*** Thermotherapy incorporating both of heat and cold has been used as a medicinal and healing modality throughout human history. Today, thermotherapy is being studied in the treatment of many diseases in most branches of medicine especially in dermatology ***(Doherty et al.,*** ***).***

I - Heat therapy:

Heat therapy is a type of treatment in which body tissue is exposed to high temperatures in order to achieve the desired therapeutic outcomes ranging from healing and repair in mild temperature elevation up to cellular necrosis and destruction of diseased or undesirable tissue in high doses ***(Doherty et al.,*** ***).***

Heat has found a great place in modern medicine, especially in dermatology. The local vasodilatation of mild heat elevation, thereby increasing blood flow and delivery of oxygen to an injured area, plays an important role in acceleration of wound healing ***(Hoffmann,*** ***).*** Induction of cellular apoptosis in medium doses and necrosis in high doses has made heat therapy an important modality in the treatment of skin tumors such as Bowen's disease, basal cell carcinoma and melanoma ***(Doherty et al.,*** ***).*** Promising results from recent clinical trials indicate also the effectiveness of heat therapy in cosmetology especially in skin rejuvenation and resurfacing ***(Bayata and Ermertcan,*** ***).***

Although the exact anti-infective mechanism of heat therapy is yet to be solved, it has shown significant results in the treatments of a variety of dermatological infectious diseases ranging from simple acne to bacterial, parasitic and viral infections ***(Doherty et al.,).*** For treatment of dermatologic infections, heat therapy can be delivered by a variety of ways ranging from hot water pads to ultrasound and even to infrared lasers particularly the CO_2 laser and Nd:YAG laser in addition to radiofrequency ***(Bayata and Ermertcan,).***

▪ Basic principle of heat therapy:

Understanding of the tissue responses to temperature variation before using a thermal agent is necessary to appropriately and effectively select the correct method, suitable temperature and sufficient time ***(Habash et al.,).***

Application of heat below the level of ٤١°C which equals the temperature of a naturally high fever helps in naturally stimulating the immunological attacks against tumor and infections ***(Stauffer,).*** Additionally, this level of temperature uses physiological mechanisms of increasing blood flow and metabolic rates, thereby safe applications in physiotherapy for treatment of rheumatic diseases, in sport medicine for treatment of ache, pain, strain, and sprain and when applied in multiple sessions for approximately an hour; it has a reparative goal of accelerated tissue healing ***(Habash et al., ٢٠٠٦).***

When the temperature of a part of the body or of the whole body is raised to a higher than normal level (٤١–٤٥°C), this is known as hyperthermia. This type of heat therapy has common applications in oncology for cancer treatment; it was found to be

effective in damaging the tumor cells by making them more sensitive to the other types of cancer treatments as radiation therapy or chemotherapy ***(Wust et al.,)***. This level of temperature was also used in the treatment of infections such as prostatitis, sexually transmitted diseases like AIDS, syphilis and gonorrhea, some dermatologic infections and others ***(Doherty et al.,)***.

Beyond the level of ٤٥°C, catabolism and irreversible tissue damage will occur. Thermal therapy with temperatures ranging from ٤٥°C to ٥٠°C results in limited tissue ablation. As a cell's internal temperature reaches between ٥٠° C and ١٠٠°C; macromolecules, proteins and DNA molecules become denatured and this lead to significant tissue ablation. Cell death results from coagulative necrosis, which occurs above ٥٠°C after two minutes ***(Habash et al., ٢٠٠٦)***. At temperatures greater than ١٠٠° C, intracellular water exceeds its boiling point, resulting in vaporization of tissue. These levels of temperature could be used for example in oncology for cancer treatment, in urology for benign prostatic hyperplasia (BPH), in cardiology for treatment of arrhythmia, in treatment of skin tumor and others ***(Stauffer and Goldberg,)***.

Tissue responses to heat are also affected by the duration of tissue temperature elevation. For example, short-duration exposure to temperature below the level of ٤٥°C leads to transitory unbalanced metabolism, and therefore unlikely to cause permanent damage. However, at the same level of temperature but for long periods (more than ٣٠ min), unbalanced metabolism could cause permanent, irreversible catabolic effect although this level of temperature is not the level of catabolism ***(Habash et al.,)***.

As previously mentioned, hyperthermia relies on a temperature below the level of ٤٥°C for periods of ٣٠ to ٦٠ min causes irreversible cellular damage. As the tissue temperature rises to ٥٠°C, the time required to achieve irreversible cellular damage decreases exponentially ***(Stauffer and Goldberg,)***.

Table (١): Effect of Temperature on Biological Tissues ***(Habash et al., ٢٠٠٦)***.

Temperature Range (°C)	Time Requirements	Physical Effects	Biological Effects
< −50	> 10 min	Freezing	Complete cellular destruction
0–25		Decreased permeability	Decreased blood perfusion, decreased cellular metabolism, hypothermic killing
30–39	No time limit	No change	Growth
40–46	30–60 min	Changes in the optical properties of tissue	Increased perfusion, thermotolerance induction, hyperthermic killing
47–50	> 10 min	Necrosis, coagulation	Protein denaturation, not subtle effects
> 50	After ~ 2 min	Necrosis, coagulation	Cell death
60–140	Seconds	Coagulation, ablation	Protein denaturation, membrane rupture, cell shrinkage
100–300	Seconds	Vaporization	Cell shrinkage and extracellular steam vacuole
> 300	Fraction of a second	Carbonization, smoke generation	Carbonization

▪ Sources of therapeutic heat energy and its therapeutic applications:

Various forms of energy in the environment impact us each day. Each form of energy falls under the category of electromagnetic radiation and can be located on an electromagnetic spectrum (EMS) based on its wavelength and frequency. The spectrum starts from the shorter wavelength relatives of the

electromagnetic spectrum family (X-rays and Gamma rays) followed by ultraviolet and visible light that can penetrate the tissue and produce photochemical reactions long before the temperature increases. On the contrary; the other part of the spectrum including infrared, microwave and radio waves have mainly thermal effect on human tissue ***(Habash et al., ٢٠٠٦).***

Scientific advances have led to the development of technologies that use the segment of EMS which have thermal effect on biological tissue and other technologies which have the same effect for therapeutic applications like ultrasound which is also considered one of the heating modalities, but it is not a part of the EMS ***(Habash et al., ٢٠٠٦).***

١. Infrared:

Infrared radiation is an invisible electromagnetic wave which can be divided according to the difference in wavelength into near-infrared radiation or IR-A (٧٦٠–١٤٠٠ nm), mid-infrared radiation or IR-B (١٤٠٠–٣٠٠٠ nm) and far-infrared radiation or IR-C (٣٠٠٠ nm–١ mm) ***(Schieke et al., ~ ~ ~).***

Penetration depth of infrared radiation in our skin is dependent on its wavelength. Near-infrared radiation is the most penetrating, it reaches some millimeters and penetrate epidermal, dermal layers and reach subcutaneous tissues, whereas middle-infrared radiation penetrates into the dermis, and far-infrared (FIR) radiation is mostly absorbed in the external layer of the epidermis and does not penetrate beyond the uppermost layer of the dead skin cells, the stratum corneum ***(Schieke et al., ~ ~ ~).***

▪ Sources of infrared therapy:

Infrared therapy can be administrated by devices capable of emitting infrared heat such as infrared lamps, infrared saunas, water-filtered infrared-A (wIRA) and infrared lasers devices ***(Doherty et al.,*** ***).***

a - Infrared lamps and saunas:

Infrared rays from infrared lamps and saunas can penetrate organic substances such as the human body without heating the air in between. Infrared radiation transfers energy that is perceived as heat by thermoreceptors in the surrounding skin ***(Kitchen and Partridge,*** ***).***

Infrared lamps and saunas have been used mainly in physiotherapy for reducing edema, muscle spasms, joint stiffness and relieving pain associated with osteoarthritis, rheumatoid Arthritis and fibromyalgia. It has been reported that regular infrared sauna therapy has also beneficial effect in reducing blood pressure, loss of weight and stimulation of immune system against viruses, bacteria and tumor ***(Oosterveld et al.,*** ***).***

b- Water-filtered infrared-A (wIRA):

Water-filtered infrared-A (wIRA) is a special form of heat radiation with a high tissue penetration and with a low thermal load to the skin surface ***(Schumann et al.,*** ***).***

Technically water-filtered infrared-A (wIRA) is produced in special radiators whose whole incoherent broad-band radiation of a ٣٠٠٠ Kelvin halogen bulb is passed through a cuvette containing water which absorbs or decreases the undesired wavelengths within

infrared (most parts of infrared-B and -C and the absorption bands of water within infrared-A). Within infrared the remaining wIRA (within ٧٨٠-١٤٠٠ nm) mainly consists of radiation with good penetration properties into tissue and therefore allows a multiple energy transfer into tissue without irritating the skin (Fig.١) ***(Hoffmann. [illegible] d).***

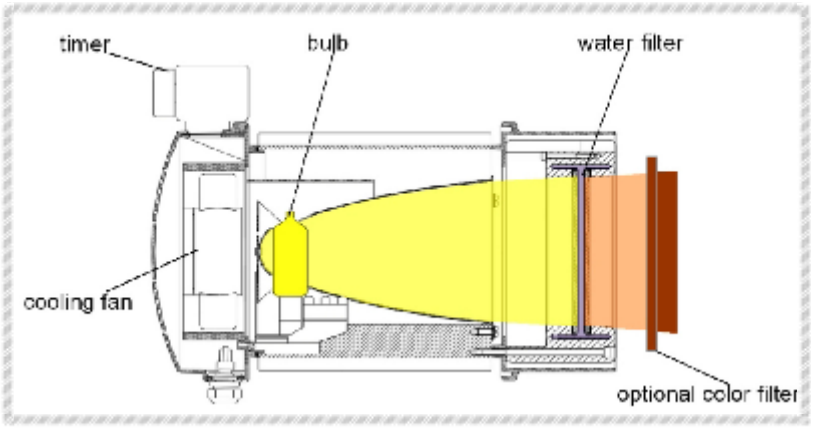

Fig. (١): Cross-section of a water-filtered infrared-A radiator. The whole incoherent broad-band radiation of a ٣٠٠٠ Kelvin halogen bulb is passed through a cuvette, containing water which absorbs or decreases the undesired wavelengths within infrared. The water is hermetically sealed within the cuvette. A fan provides air cooling of the cuvette to prevent the water from boiling ***(Hoffmann. [illegible] d).***

Water-filtered infrared-A increases tissue temperature (٢,٧ °C at a tissue depth of ٢ cm), tissue oxygen partial pressure and tissue perfusion. These three factors are decisive for a sufficient supply of tissue with energy and oxygen and consequently also for wound healing and infection defense ***(Schumann et al., [illegible]).*** Water-filtered infrared-A can considerably alleviate the pain and also it can be safely and effectively applied to heat localized superficial tumors (up to ١ cm depth) to increase the efficacy of external beam radiotherapy (Fig.٢) ***(Seegenschmiedt et al., ١٩٩٦).***

Fig. (٢): Infrared heat therapy with wIRA ***(Schumann et al.,)***.

c- Infrared lasers:

Lasers fall in the infrared spectrum of light which are commonly and successfully used in medicine include; CO_2, Er:YAG, holmium, Nd:YAG and diode lasers. These types of laser typically emit an invisible infrared beam at ١٠،٦٠٠ nm, ٢٩٤٠nm, ٢١٠٠nm ,١٠٦٤nm and ٨١٠ nm respectively (Fig.٣) ***(Alster and Lupton,)***.

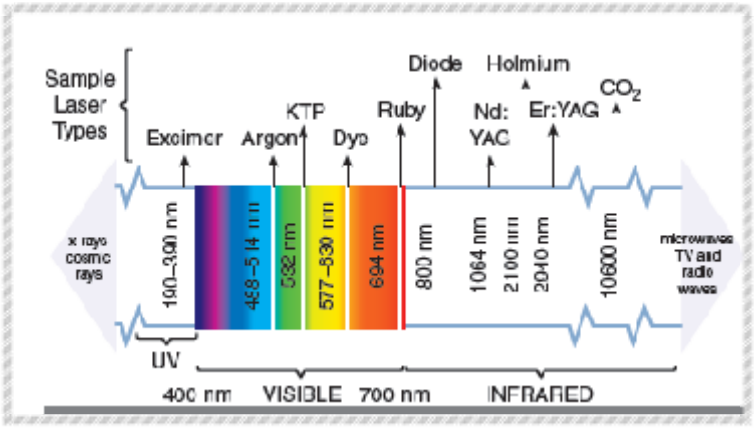

Fig. (٣): The most common laser identified in the visible and infrared portion of the electromagnetic spectrum radiation ***(Alster and Lupton,)***.

Different types of laser including visible and infrared lasers have different tissue effect such as photothermal, mechanical and photochemical effect. By far, the most important interaction is the photothermal especially for dermatologists ***(Lanigan,)***.

Most therapeutic effects of lasers are seen as cellular reactions to thermal laser energy. As the laser's radiant energy comes in contact with tissue, the light is absorbed by its target chromophore and transformed to heat (Fig.٤). This is the primary mechanism by which lasers function in skin. The three main chromophores in the skin are melanin, hemoglobin and water ***(Tanzi et al.,)***.

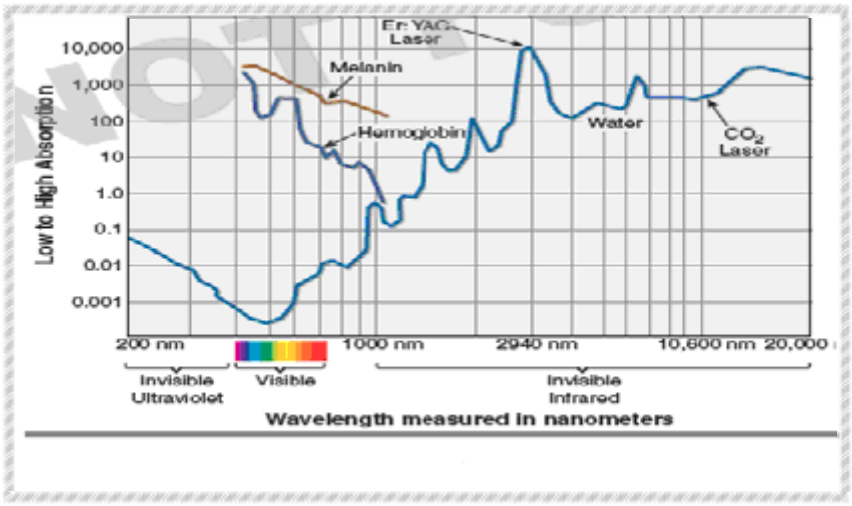

Fig. (٤): Absorption spectra of the three main skin chromophores ***(Tanzi et al.,)***.

Depending on the actual temperature achieved within the target, various effects can occur. A temperature increase in the tissue of only ٥°C can lead to tissue injury with subsequent inflammation and repair. At temperatures above ٦٠°C, a denaturation of proteins and DNA and a coagulation of the tissue

occur. Finally, at temperatures above ١٠٠°C, the intracellular water exceeds the boiling point and vaporization occurs, which can be seen clinically as ablation of the tissue ***(Lanigan,)***.

The theory of selective photothermolysis states that laser energy can be absorbed by a defined target chromophore leading to its controlled destruction without significant damage to the surrounding tissue. Based on concept of selective photothermolysis; the wavelength, pulse duration and fluence must all be tailored to the properties of the target chromophore and clinical indication in order to produce a desirable clinical outcome and avoid complications ***(Shaffer,)***.

The wavelength of the laser light needs to correspond to the absorption maximum or lie within the absorption spectrum of the respective target chromophore ***(Alora and Anderson,)***. The pulse duration, also called 'pulse width' of the laser beam must be equal to or shorter than the thermal relaxation time (TRT) of the target chromophore. The TRT is defined as the time needed for the target chromophore to dissipate ٦٣٪ of its peak temperature.This time is directly proportional to the square size of the chromophore ***(Stratigos and Dover,)***. The energy density delivered by the laser beam, also referred to as fluence, must be high enough to actually destroy the target chromophore within the defined pulse duration. Energy densities are measured in joules per centimeter squared (J/cm٢) ***(Shaffer,)***.

The use of the laser requires additional awareness of the power distribution within the impact spot. Power density (Pd) is defined as the energy delivered per unit area of incident tissue. It is measured in terms of wattage of laser per diameter of the beam.